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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,041	04/02/2001	Ralf-Christian Schlothauer	DAIRY64.001A	6853

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EXAMINER	
PRATS, FRANCISCO CHANDLER	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,041	SCHLOTHAUER ET AL.	
	Examiner	Art Unit	
	Francisco C Prats	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-36,39-50,59 and 62-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *59* is/are allowed.

6)☒ Claim(s) *32-36,39-50 and 62-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12-8-03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed April 23, 2004, has been received and entered. The Declarations of Sophia Stathopoulos and Julian Robert Reid have been received and considered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 32-36, 39-50, 59 and 62-68 are pending and are examined on the merits.

Claim Rejections - 35 USC § 102

Claims 32, 33, 35, 44, 45, 50 and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Mullally et al (Int. Dairy Journal 7:299-303 (1997)).

Mullally discloses a process whereby whey protein concentrate containing 4.7% lactose (see page 300, paragraph entitled "Substrates") is contacted with protease at a temperature of 50 degrees C at a pH of 8 to a degree of hydrolysis ranging from 0 to 8% (see Fig. 1, page 301), followed by heat inactivation of the enzyme (see page 300, paragraph entitled "Pilot-scale hydrolysis of WPC"), followed by assaying of ACE inhibitory activity (see, e.g., Fig. 1, page 301). Mullally also processes the resulting hydrolysate by

ultrafiltration with a 10 kD cutoff membrane. See, e.g., Table 2 on page 302. Mullally therefore anticipates the cited claims.

Note that Mullally is considered to anticipate claim 50 because the same substrate as claimed is contacted with the same enzyme as claimed under the same conditions as claimed to make a product having the same degree of hydrolysis as recited in the claims. The resulting product must therefore be the same. If there is a difference between the prior art and the claims, it must be due to some aspect of the process not recited in applicant's claims.

Lastly, it is noted that as amended claim 32 and its dependents now require the hydrolysate to be able to be spray dried. Because the ultrafiltered hydrolysate of Mullally can be spray dried, Mullally's process meets the new limitation.

Claim Rejections - 35 USC § 103

Claims 32-36, 39-45, 50 and 62-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mullally et al (Int. Dairy Journal 7:299-303 (1997)) in view of Abubakar et al (Tohoku Journal of Agricultural Research 47(1-2):1-8 (1996)).

As discussed above, Mullally discloses a process whereby the whey protein concentrate is hydrolyzed by proteases and the resulting hydrolysate is tested for ACE inhibiting activity.

Mullally differs from the claims in failing to use the claimed proteases. See applicant's claim 34. However, in view of the combined disclosures of Mullally and Abubakar, demonstrating that a large variety of proteases having different specificities all result in the production of ACE-inhibiting peptides from whey protein, the claimed use of commercially available proteases must be considered obvious under § 103(a).

Further still, the determination of suitable parameters for heat and/or pH-based enzyme inactivations (applicants' claims 36, 39 and 40) for the processes of Mullally and Abubakar would have been obvious in view of the fact that such methods of enzyme inactivation are notoriously well known in the enzymology arts, the determination of suitable or effective parameters in such processes being routinely optimized by those skilled in the art. Still further, the use of immobilized enzymes (applicant's claims 42-44) is well known in the art, and would have been obvious in view of the disclosures of Mullally and Abubakar.

Further still, the use of the hydrolysates of Mullally in the treatment of hypertension, encompassed by claim 62, clearly would have been obvious in view of the disclosure of both Mullally and Abubakar that protease-hydrolyzed whey hydrolysates possess ACE-inhibiting peptides. Still further, although neither Abubakar nor Mullally disclose the use of chromatography

in the separation of peptides (applicant's claims 64-67), Mullally clearly discloses that using filtration to fractionate the hydrolysates on a molecular weight basis filtration results in fractions having differing, and in some cases increased, anti-hypertensive activity. Thus, Mullally clearly discloses the desirability of fractionating protease-digested whey on a molecular weight basis. The artisan of ordinary skill, recognizing at the time of applicant's invention that high performance liquid chromatography (HPLC) was a well known method of fractionating protein mixtures on the basis of molecular weight, clearly would have considered HPLC a suitable method of separating Mellqvist's whey hydrolysate on a molecular weight basis, so as to isolate those peptide fractions containing increased anti-hypertensive activity, said fractionation being taught by Mullally as being advantageous. A holding of obviousness over the cited claims is therefore required.

Claims 32-36, 39-50 and 62-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mullally et al (Int. Dairy Journal 7:299-303 (1997)) in view of Abubakar et al (Tohoku Journal of Agricultural Research 47(1-2):1-8 (1996)), and in further view of Soehnlen (U.S. Pat. 4,358,464).

As discussed above, Mullally viewed in light of Abubakar renders obvious the process recited in claim 32, as recited in embodiments present in certain dependent claims. Mullally and Abubakar differ from the claims in that those references do not disclose the use of β-galactosidase in treating the whey product, as recited in claims 45 and 49. However, Soehnlen discloses that the use of β-galactosidase in treating a whey product, improves the taste of the product. See abstract. Thus, the artisan of ordinary skill, recognizing from Soehnlen that β-galactosidase was useful as a method of removing undesired lactose from the whey starting material or peptides resulting from the processes of Mullally and Abubakar, clearly would have been motivated to have used β-galactosidase in Mullally and Abubakar's processes to further improve the purity of the resulting product. Claim 49 must therefore be considered obvious over the cited references.

Response to Arguments

All of applicant's argument has been fully considered but is not persuasive of error. It is recognized that the Stathopoulos and Reid Declarations evidence great diligence, expense and effort. However, at the outset, it must be pointed out that the process in Mullally differs somewhat from the

processes documented in the declarations. Specifically, Mullally uses an 8% w/v whey solution for hydrolysis, whereas the declaration and specification use a 15% w/w solution of whey. It is further noted that Mullally uses a different whey starting material, "Lactalbumin-80", than used in the demonstrations. More to the point, however, is the fact that the Mullally article describes every limitation in claim 32.

As discussed above, Mullally hydrolyzes the same starting material under the same conditions recited in the claims, inactivates the hydrolytic enzymes with heat, and then tests for ACE-inhibiting activity. With respect to the new claim language requiring the inactivation to yield a product which can be spray dried, it is again pointed out that Mullally et al subjected their hydrolysate to an ultrafiltration step before testing for ACE-inhibiting activity. Mullally's ultrafiltered hydrolysate is a "water soluble hydrolysate that can be spray dried" as recited in claim 32.

Note specifically that claim 32 recites the process in open "comprising" language. This language does not exclude additional process steps, such as the ultrafiltration step in Mullally, as evidenced by the recitation of precisely such an ultrafiltration step in applicant's claim 41. Mullally's ultrafiltration step produces small soluble peptides. For

example, as pointed out in item 11 of the Reid declaration, the "small and medium sized peptides in [Mullally's] hydrolysate which express ACE inhibiting activity are soluble[.]" Thus, applicant's own Declaration provides evidence that Mullally's process yields products meeting the claim limitation requiring the enzyme inactivation to yield a water soluble hydrolysate that can be spray dried.

In sum, the Stathopoulos and Reid Declarations provide evidence that the 80°C/20 minute inactivation step of Mullally's process may provide an insoluble, largely unusable, denatured coagulum. However, Mullally's process also comprises an ultrafiltration step yielding a water soluble hydrolysate which can be spray dried, said ultrafiltration step being encompassed by the current breadth of applicant's claim language. Because applicant's claims do not possess language sufficiently distinguishing them from Mullally, and because applicant's claims are sufficiently broad to encompass the process disclosed by Mullally, a holding of anticipation remains required.

As to the commercial non-viability of Mullally's process asserted by applicant in the response and Declarations, it is noted that none of the claims contains any limitation requiring any particular absolute or percent yield. Thus, to the extent that applicant argues that their process provides an increased

yield over Mullally's process resulting in commercial viability, applicant's claims are not commensurate in scope with this argument. Moreover, Mullally suggests the commercial potential of his process by naming the larger hydrolysis process a "pilot-scale" process, and by discussing the commercial advantages of whey-derived peptides compared to commercially available hypertension-treating drugs on page 302.

With respect to the issue of the obviousness of a specific duration for the heat inactivation of the enzyme, it is respectfully pointed out that only claim 36 recites a specific duration for the inactivation. As pointed out above, such methods of enzyme inactivation are notoriously well known in the enzymology arts, the determination of suitable or effective parameters in such processes being routinely optimized by those skilled in the art. Thus, as to the ability of the artisan of ordinary skill to determine such suitable enzyme inactivation conditions, it is maintained that one of skill in the art, recognizing that Mullally's process requires an enzyme inactivation step, would have been readily able to determine suitable conditions therefor. Applicant's assertion that no support has been offered for this proposition is especially confusing in view of the fact that certain assumptions must be made about general knowledge in the art, and is doubly confusing

in view of the IDS submitted December 8, 2003. The sole document cited in this IDS demonstrates the routine nature of determining enzyme inactivation conditions. Thus, it is not clear why applicant suggests that determination of a suitable enzyme inactivation protocol was not routine, since applicant clearly recognizes the proposition to be accurate. Absent some unexpected result coming from the enzyme inactivation protocol recited in claim 36, claim 36 must be considered an obvious variation on the Mullally process. The artisan of ordinary skill practicing Mullally's process would have been motivated to have used any enzyme inactivation method which would have functioned in that process.

Lastly, with respect to claim 62, it is respectfully pointed out that the claim encompasses combinations of the peptides, and that such combinations read on the peptides produced by Mullally.

Claim 59 is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this

action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 571-272-0921. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Francisco C Prats
Primary Examiner
Art Unit 1651

FCP